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MINUTES OF EVIDENCE
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THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY II

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ZENECA

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GLAXO GROUP RESEARCH LIMITED

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Present:

Flowers, L.
Hilton of Eggardon, B.
Howie of Troon, L. (Chairman)
Perry of Walton, L.
Renwick, L.
Soulsby of Swaffham Prior, L.
Whaddon, L.

Written Evidence from Zeneca

1. *What is your interest in biotechnology?*

Zeneca is a fully owned subsidiary of ICI and has four businesses (pharmaceuticals, agrochemicals, seeds and speciality products) which are fully involved in exploiting the opportunities offered by biotechnology. The company employs 33,000 people and had sales of almost £4 billion in 1992. Zeneca invests heavily in the research and development of new products, the enhancement of its existing range and the improvement of manufacturing efficiency. Biotechnology is a fast moving area of research which provides a unique set of tools which Zeneca is making full use of in each of its businesses. In 1992 Zeneca spent £457 million and employed 7,000 staff on research and development; the majority of this expenditure was in the U.K. The extent of Zeneca's use of biotechnology is illustrated in the article reproduced as Annex 1. (*not printed*)

2. *How and why is biotechnology important to U.K. industry?*

In the coming years biotechnology offers opportunities for economic growth in the health care, chemical, agricultural and food sectors. These are sectors where British industry has traditional strengths, and which make a significant contribution to the wealth of our country. In the next decade the British consumer will increasingly be offered, and will also demand, products which have been produced using biotechnological techniques; it is essential for the future prosperity and prestige of this country that as many of these products as possible are developed and manufactured by U.K. industry.

3. *What future prospects and opportunities does the technology offer?*

The techniques embraced by the term biotechnology will be the next major source of innovation in the above mentioned industries.

The invention of new drugs, agrochemicals or the breeding of new plant varieties in the 1990s requires, more than ever, a molecular insight into the functioning of genes, cells and tissues. The skills of those trained in biotechnological techniques now complement the established research disciplines in the pursuit of effective solutions to the challenges facing our society. These challenges include finding cures for cancer and diseases of the ageing, reducing the environmental impact of our activities or providing better quality food.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

Our ability to transfer genetic material between different species (genetic modification) and the ability of these genetically modified organisms (GMOs) to self-replicate is often cited as a cause of concern, for example that man will inadvertently create new pathogens or weeds. We find arguments that genetic modification is inherently safe are as unhelpful as arguments that all genetic modification is dangerous and should be stopped. What society needs is a science based regulatory system, that is strictly enforced by a regulatory authority. Such a system would encourage research and investment and would help develop the confidence of the public.

We believe that the U.K. until the late 1980s was developing a regulatory system that protected both man and the environment while encouraging investment in research and industry. However, the debate over the last few years on the implementation of European Directives 90/219 and 90/220 has impeded the conduct of research and development in both academic and industrial sectors and there is no evidence that safety has been increased. This is because the Directives appear to be based on the concept that genetic modification *per se* poses unique risks to man and the environment and therefore must be controlled in a unique manner. In addition to the damage to our academic and industrial competitiveness, the debate has done nothing to build public confidence in the regulatory system. We develop these arguments in the following sections.

The design of the risk assessment procedure is fundamental as this will establish the type of controls needed. We believe that assessment of risk should:

— Recognise that genetic modification work on viruses, bacteria, fungi, plants or animals poses different potential safety issues because these organisms are so different from each other.

— Accept that work during the research, development and commercialisation phases or in a laboratory, factory, glasshouse or field trials, poses many different potential safety issues.

— Build up confidence on a case-by-case approach with a combination of risk assessment and monitoring.

— Take account of existing knowledge, for example, about the usual behaviour of crop plants.

— Acknowledge the considerable body of experience gained by successful genetic and modification work.

— Be concerned with the objectively measurable criteria of safety, quality and efficacy.

The above would allow rapid progress to a situation where regulatory attention and resources could be focused upon developments which pose a real risk.

Over nearly 20 years, genetic modification in the U.K. and world-wide has had an exemplary safety record. Where safety issues arose during the application of the technology, for example during discovery research or process development, then they were handled effectively and safely by existing legislation. Examples of such legislation are the Health and Safety at Work Act (HASAWA), the Control of Substances Hazardous to Health Regulation (COSHH) or the Genetically Modified Organism Regulations of 1989. When safety issues arose with a product which was also a GMO then the appropriate product regulations were applicable.

We believe that for the United Kingdom the Advisory Committee system has proved to be an effective way of regulating biotechnology. The Advisory Committees for Genetic Modification (ACGM), Release into the Environment (ACRE) and Novel Foods and Processes (ACNFP) have provided a forum where scientific advice can be gathered and the evidence concerning a particular issue reviewed by a broad representation including "lay" involvement (representatives of the employers, trade unions, local government etc.) Such experience would develop along the lines of work with unmodified organisms, which are controlled by the Advisory Committee for Dangerous Pathogens (ACDP) guidelines. It is interesting to note that these guidelines are less restrictive than the new Genetically Modified Organisms (contained use) Regulations despite the fact that genetic modification work is normally based on non-pathogenic micro-organisms and known gene sequences of known properties.

5. *Should biotechnology be regulated by an industry specific regime?*

There is no such entity as a biotechnology industry, therefore there is no need for a biotechnology industry specific regulatory regime. However, there are sectorial industries which employ biotechnology and are already regulated for safety, quality and efficacy. For example, genetic modification may be used in the production of, flowers, potato tubers, yoghurt, bread, potato crisps, anti-rabies vaccine, anti-cancer drugs. Each of these products raises its own safety questions. It is therefore in our view axiomatic that each class of products requires its own specific evaluation and should hence be regulated by the appropriate specific regulatory regime. These sectorial based regulations will of course evolve to accommodate new technology if it changes the essential nature of the product.

6. *From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than a vertical regulation (where a product is judged by its characteristics)?*

The key question is whether the trigger for the regulatory review should be the act of genetic modification or the product. There are three broad areas for regulation: laboratory research, the development period (trials etc.) and placing a product on the market. The first can be realistically handled by regulations concerned with protection of the worker and, if appropriate, protection of the environment. However, once one has actually used the techniques to produce a potential product then there is a clear difference of opinion on how to regulate. The European Community produced Directive 90/220 which uses as a trigger for regulatory review the act of genetic modification. In the USA existing legislation was adapted to deal with the development and marketing of products produced by genetic modification.

The vast majority of scientific opinion supports the product approach. For example:

In Ecology (1989), 70, 297-315, prominent ecologists summarised the critical issues surrounding the release of genetically modified organisms. One of their key recommendations was that GMOs "should be evaluated and regulated according to their biological properties (phenotypes), rather than according to the genetic techniques used to produce them".

Brill in "Issues in Science and Technology" (1988) notes that we have considerable experience with organisms that are modified by traditional techniques. In most cases the nature of the genetic modification achieved by these traditional techniques has been far more dramatic than that accomplished by recombinant DNA technology.

The National Research Council (1989) published a report on Field Testing of genetically Modified Organisms. For crop plants they concluded that "crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits. As the molecular methods are more specific, users of these methods will be more certain about the traits they introduce into the plants. Traits that are unfamiliar in a specific plant will require careful evaluation in small-scale field tests where plants exhibiting undesirable phenotypes can be destroyed." The paper also proposes that as our

knowledge increases, entire classes of introductions (of GMOs) may become familiar enough to require minimal oversight.

Super-imposing a horizontal regulatory approach upon a vertical regulatory system will not lead to any increase in safety for human health nor in the environment.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

Horizontal regulations are appropriate where the application of a technology raises safety issues. Vertical regulation is appropriate where the product is being developed or commercialised.

In the medicinal product sector, it is hoped that the EEC will follow the USA model to a degree by permitting the assessment of safety under 90/220 to be conducted by the medicines agency as a part of the assessment under the medicines directives.

Gene therapy offers considerable benefits in the treatment of diseases. Over the last five years there has been an extensive review of the technical, safety and ethical issues concerning gene therapy both in the USA and in the EC. Currently, there are stringent regulations governing the application of somatic gene therapy. We believe that any relaxation of these regulations will depend on the experience gained from the first batch of trials. Zeneca endorses this regulatory approach.

8. *How do current regulations compare with those of competitor countries*

In 1990 the EEC passed two Directives covering biotechnology: one for contained use of GMOs (90/219), the other for the deliberate release to the environment and marketing of GMOs (90/220). However, the EEC Communication "Promoting the Competitive Environment for the Industrial Activities Based on Biotechnology Within the Community" which defines the policy for biotechnology in Europe and hence the role of regulation has not yet been debated in the European Parliament. Member States should have implemented Directives 90/219 and 90/220 into National legislation by October 1991. Many Member States are finding it difficult to implement these Directives. In the U.K. the regulations which implement the Directives had to undergo extensive modification after the first round of consultation because of their inappropriate and grossly convoluted format.

It is valuable to contrast the development of the two major regulatory influences on biotherapeutic manufacturing in the U.K., ie the European Guidelines on Good Manufacturing Practice and the EC Directive 90/219 on the contained use of genetically modified organisms. The former regulations evolved over 30 years through close co-operation between the pharmaceutical industry and the regulatory authorities. Standards in concept, design and engineering practice have been developed which are universally recognised and accepted. On the other hand, the new regulations on containment of processes involving recombinant organisms which have been imposed on the industry, are sufficiently vague in defining what is actually required in practice to cause uncertainty.

The Directive 90/220 imposes a horizontal based regulatory approach on the commercialisation of products. This approach has inevitably led to arguments over:—

- — definitions, ie what actually is, or is not, meant by genetic modification
- — excessive bureaucracy, though at last there are some discussions between the European Commission and Member States to develop "simplified procedures" for the Deliberate Release Directive which will try and remove unnecessary regulatory burdens for certain types of genetically modified crop plant. These changes are occurring even though the Directives have not been implemented in all Member States.
- — conflicts with existing vertical regulations which is leading to the rewriting of vertical regulations and directives in an attempt to develop a workable vertical or product-based system. For example, we understand that Directives or Regulations on Patents, Novel Food Ingredients, marketing of Genetically Modified Farm Animals, marketing of New Varieties of Plants, Transport of Genetically Modified Organisms are now being prepared. Simply transferring the requirements of Directive 90/220 into vertical regulation may be an administrative solution, but we fear that this will be a case of "building a house upon the sand".

The complexity of, and the confusion, caused by these Directives is sending a very negative message to the academic, industrial and financial communities. More seriously public confidence in the regulatory systems is being damaged.

Special legislation for regulating genetic modification was not developed in the USA. Their regulatory system is based on existing legislation which covers, for example crop plants and food, the logic for their approach is outlined above. This has had two advantages:—

- — the degree of regulatory oversight can be easily modulated in the light of experience.
- — there is no disruption of the existing product legislation.

The result is that both the industry, and in our experience the majority of the public have confidence in the regulatory system

The United States Department of Agriculture has recently, after holding public hearings, proposed that the present system requiring permits issued by the USDA should be replaced by a notification system for field trials with certain crops (corn (maize), cotton, potato, soybean, tobacco and tomato) when the genetic material inserted is well characterised.

In essence, although U.K. biotechnology regulation is seen to be at neither extreme of the implementation of 90/219 and 90/220 in Europe, European biotechnology overall is greatly disadvantaged with against that of USA and Japan.

9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the U.K. industry, in particular as regards*

1. *research*
2. *product development*
3. *investment*
4. *location*
5. *sales and marketing?*

Zeneca Pharmaceuticals currently estimates that its genetic modification safety costs will rise by approximately 50 per cent to meet the new regulations. Additional capital expenditure of 5—10 per cent is required for normal research activities, while this will rise to 25–30 per cent for certain larger scale activities. Similar costings are predicted by the other Zeneca businesses.

At the present time, Zeneca Pharmaceuticals is producing all material for clinical and preclinical testing within the U.K. either in-house or through contractual arrangements. Where Zeneca will manufacture in the future has not been decided. It is, however, clear that the evolving regulatory climate and attitudes in European Community will make a significant contribution to this decision. For example, in Germany difficulties on the regulatory front have led several companies to build their facilities in the USA. The incoming investment that is being attracted into Europe is, at the moment, largely going outside the U.K.: in particular to the Republic of Ireland and to the Netherlands.

Zeneca Seeds carries out research in Argentina, Belgium, U.K. and the USA and has carried out field trials with genetically modified crop plants in Australia, Belgium, Canada, Chile, U.K. and USA (California, Florida and Iowa). There is an increasing cost of carrying out field trials in the U.K. For example, to obtain permission for a four hectare field trial in California requires under 25 per cent of the paper work required for a 400 square metres field trial of oilseed rape in the U.K. As noted above when the proposed USDA system is adopted a notification letter will be all that is required for the American field trials.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the U.K. science base?*

The U.K. biotechnology research base has been first rate and industry is developing many of its ideas. For example, some of the research at the Universities of Cambridge, Edinburgh, Leicester, Nottingham, Oxford and Warwick has been, or is being, developed by Zeneca. This research is creating jobs and wealth in the U.K.

We would like to repeat part of the summary of the views expressed by ICI on the forthcoming Government White Paper on Science and Technology.

> "Innovation for World Markets is needed to prevent terminal decline of U.K. manufacturing industry.
>
> Leaving aside all special pleading, the U.K. science base is substantially underfunded.
>
> We cannot afford everything and must give greater reinforcement to those areas of science and technology which are inherently more exploitable and where we have some sort of national advantage."

In the biotechnology area the U.K. has a commendable record of both research and industrial achievement. From the above paragraphs it is clear that we have serious concerns that the costs associated with over-bureaucratic regulations in the U.K. and Europe will damage University research. This will make the U.K. a less attractive prospect in the future for companies such as Zeneca.

11. *How best can issues of public acceptance be addressed?*

The public perception of biotechnology varies considerably from country to country and between product sector.

Biotechnology will not be used by British industry if society or the consumer does not want the resulting products. The question is, therefore how to provide the public with the information they need to make a decision.

Non-governmental organisations have a role to play and industry, university and research institute scientists must be prepared to provide the answers to their questions. We have found dialogue with many of these groups to be very productive. However, we have to accept that there are some extreme pressure groups who are simply opposed to biotechnology. In the U.K. these extreme groups have not yet had the degree of negative influence on the image of biotechnology that has been achieved by their counterparts in, for instance, Germany. Were the lobbying and scare-mongering of the extreme pressure groups in the U.K. to gain the upper hand then doubtless the serious problems being faced by academia and industry in Germany would occur here.

In order to encourage public confidence there is a need for a focused campaign aimed at explaining to the public in honest, non-scientific terms the technology, the regulatory safeguards and the benefits arising from each sector of biotechnology. There is also the need for a source of information which in the view of the public offers a factual and unbiased service. We believe that this is the role of organisations such as the COPUS, the Science Museum and the National Centre for Biotechnology Education at the University of Reading; these organisations require government funding.

Regulation has a critical function to perform in this context. The right level of regulation will reassure the public but inappropriate regulation would not satisfy public confidence and would severely damage the efforts and prospects of those industries where biotechnology is an ever increasingly important tool.

12. *What other factors do you consider will play a crucial role in the competitiveness of the U.K. biotechnology industry?*

Beside the impact of an excessively bureaucratic regulatory regime in the U.K. we consider that the following factors are also undermining the future competitiveness of our activities which are dependent on the application of Biotechnology:

(a) Intellectual property rights:

The genetic modification of organisms has raised a number of new issues regarding patent rights. The main problem at present is that very broad claims are being granted by the European Patent Office (EPO); it is difficult to see how these broad claims are justified by the actual invention made by the patentee. This means that the rest of industry is held up by those claims unless licenses are granted. Improved training of examiners at the EPO in this fairly new area of technology could help to avoid this problem: though, more fundamentally there is a question of whether the EPO's approach gives the proper balance between the rights of the patentee and those of the public.

A problem of unfair competition which is not unique to biotechnology is the US practice of granting claims to the first party to *invent in the USA*, which places non-US inventors at a significant disadvantage: but there are prospects that this will be resolved by a Patent Harmonization Treaty.

The Directive concerned with the patenting of biotechnological inventions has been the cause of extensive debate in the European Parliament and is now in the hands of the Council. Zeneca needs legislation which offers adequate protection for our large research investment in biotechnology research. The general response of industry to the proposed legislation is that it fails to achieve this, and indeed would create damaging precedents with Farmer's privilege and compulsory licensing; it also does not conform to the current GATT-TRIPS proposals.

(b) Funding of basic research:

Historically the U.K. has much of which to be proud in regard to the basic discoveries which have stimulated modern biotechnology. The structure of DNA, the unravelling of the genetic code and the discovery of monoclonal antibodies are attributed to U.K. laboratories. As noted above, Zeneca seeks to work with Universities in basic research in the belief that this will lead to innovative products. Basic research is very costly and it is imperative that the U.K. ensures adequate support for this work either directly or through effective competition for EC programme funds.

(c) Education:

The creation of an increased level of awareness in schools and universities of the positive contributions of biotechnology to health and national prosperity will achieve two critical goals. Firstly it should help to counteract any fear of biotechnology that arises through ignorance within society at large. Secondly it is essential to support the creation of an adequately trained scientific workforce to deliver what we hope will be a significant contribution to the U.K. economy from the application of biotechnology.

Examination of witnesses

DR ED DART, Zeneca Seeds Research Director, MR G MUSKER, Company Secretary and PROFESSOR N J POOLE, External and Regulatory Affairs Manager, Zeneca Seeds, called in and examined.

Chairman

177. Good morning, gentlemen. Welcome. I think some of us had the pleasure of meeting some of you down at Jeallot's Hill a few weeks ago where you gave us a very full presentation of these matters. Would you like to say something to us in general, introducing your colleagues, Dr Dart?

(*Dr Dart*) Thank you very much, Lord Howie. My Lords and Ladies, we are delighted as Zeneca to be given the opportunity to speak to you today. I would like to start by introducing my two colleagues here: Dr Nigel Poole who is the Regulatory and External Affairs Manager for Zeneca Seeds who has a lot to do with biotech regulatory issues and Mr Graeme Musker who is the Zeneca Company Secretary, who is here to keep us honest! I am research director of Zeneca Seeds but also play a role in co-ordinating biotechnology across all of our bioscience research. As you will see from our submission the biologically based businesses in Zeneca cover pharmaceuticals, crop protection, seeds and biological products. Biological products cover applications of biotechnology outside of the health care and agricultural fields. We believe biotechnology is vital to the development of all of these business. In pharmaceuticals it gives us access to or the option to create new protein drugs. Worthy of mention here is one in Phase I clinical development for the treatment of colorectal cancer which at the moment is a non treatable disease. In our view the main impact of biotechnology in pharmaceuticals will be in facilitating the invention of new synthetic small molecules drugs through greater understanding of biological systems and in designing smart screening procedures that will help us identify more active molecules in a more efficient way. In crop protection the story is somewhat similar. We are interested in the isolation and design of biological control agents for some pest and disease applications but also in using the extra understanding that the new bioscience techniques give us to help us design new synthetic active ingredients that are safer, used in lower doses and more environmentally friendly than those currently in use. In seeds we entered the business in the belief that the plant breeding process was going to be changed by the application of biotechnology both in making selection more efficient and in helping the plant breeder to have access to novel sources of genes. We believe both of these aspirations are coming true. In our biological products business we have products like Quorn, our microprotein processing foodstuff—which some of you tasted when you visited—and Biopol, a biodegradable plastic. We also use biological systems to make molecules that organic chemists find it difficult to make in economic amounts themselves by a process called biotransformation. We are also interested in the use of micro-organisms as what are called bioremediation agents, for cleaning up contaminated waste and soils. So as you can see we have a fairly extensive interest in the technology. Alongside this we have made contributions to the developments of GMO regulations in the United Kingdom. ICI and Zeneca has always had representatives on the Advisory Committee of Genetic Manipulation and its precursor groups. We also have representation on the Advisory Committee on Release to the Environment and the Advisory Committee on Novel Foods and Processes. We have always been impressed by the way that these groups have managed the evolution of the technology and balanced it with perceived risk. Our concerns began when the European Commission introduced its Directive 219/220 and in our view did not give credence to the views of experts in this industry. We were then not organised as a European industry to give a collective response to 219 and 220. To ensure our collective voice was heard we and other major European companies, with the agreement of the rest of the European industry, formed the Senior Advisory Group on Biotechnology whose aim was to ensure that the Commission was aware of industry's concerns in developing biotechnology regulations. Dr Poole will say more on SAGB later. Our stance on regulations is that we need them. If Government were not to have them we would impose them on ourselves. But in our view regulations have to be soundly scientifically based and should evolve in a more or a less stringent way depending on how experience develops. In summary I would say this technology is of great importance to us and we believe both to us and to Europe's economy. It offers us novel cures to difficult diseases like cancer, Alzheimers and arthritis and the prospect of correcting genetic defects. In agriculture we can see prospects for crops with enhanced quality and resistance to stress, pests and diseases as well as offering new strategies for crop protection. The prospect is also there for the extension of agriculture to producing novel feedstocks and products for both the chemical and food industries. So it is a technology that we are excited about but we are determined that we will progress under the regulatory regimes that are imposed by the various governments of the world. That is all I would like to say as an introduction.

178. Thank you. Before we go into detail, can I ask you a general question: I am told the DTI has established seven de-regulation task forces of one sort or another. I think one of them at least impinges on your area of activity, are you aware of this and do you intend to make any submissions to the task force?

(*Dr Dart*) Perhaps Dr Poole can answer after me but we are aware that these task forces are set up and we are delighted that there is a watchdog on the regulator, if you like, because I do think that is a very important thing to have so regulations do change with the way that perceived risks develop. We have not as yet decided whether or not to make a submission to this group.

(*Professor Poole*) Just one point about the name, we are not looking for no regulations, we are looking for the appropriate level of regulations. We shall make evidence I am sure when asked.

[**Chairman** *Cont*]

179. When you make submissions for consents and so on, do you get any help from the DoE or the Health and Safety Executive in drawing up your submissions?

(*Dr Dart*) To, for example, the DTI?

180. Yes?

(*Professor Poole*) Submissions to do an experiment?

181. Yes?

(*Professor Poole*) We find the Health and Safety Executive and the DoE are very helpful, you know who to ring up and they will give you advice and we take it.

182. Do you discuss your submission with them before you put it in?

(*Professor Poole*) We try to understand the questions to be asked and the answers, then we put together our submission, then it is up to the DoE and HSE to progress it.

183. You mentioned SAGB, could you tell me what it is and what its achievements are?

(*Professor Poole*) As you have seen from our submission one of our arguments is that biotechnology is a set of tools which covers a very wide range of sectors, four or five sectors in our business alone. The problem then is that there is a large number of industrial associations and federations both in the Member States and in Brussels, all interested in biotechnology. The message we got from the Commission and from our own soundings was that we needed a co-ordinated voice. So the SAGB was formed three or four years ago with the objective of providing that senior umbrella organisation to provide that brief. Its functions are to co-ordinate input into the Commission and to the Council of the right sector groups so they know who to ask and to call in effect. It is clear from our submission—and I am sure the submissions of other companies—that biotechnology is the next driving force for innovation in the European industry. I think the SAGB can claim some success for that realisation which is dawning in the Commission of the importance of biotechnology. We saw that a year ago with the publication of the policy of biotechnology for European industry. I think there are other things about SAGB. As we are all moving towards the new Europe, the new Single Market, industry is having to learn how to relate to the European institutions and the SAGB is an experiment in how to relate to the European institutions and I think a very successful one. It is a model which has been followed in other sectors already. I think it has also helped bring some of the expertise into the Commission and into the Council. We have been able to identify people who know what the subject is and they have been able to help advise the Commission so I think it has helped the Commission as well.

184. You think it is a thoroughly useful body then?

(*Professor Poole*) It has been an extremely useful body, yes.

(*Dr Dart*) I think part of the measure of that is it started with seven large European companies and the membership now is what, Nigel?

(*Professor Poole*) It is about 34 large and small companies. It is not an association of everybody, it is an association of companies who are doing major research or development in the European Community so it is large and small companies and all Member States.

(*Dr Dart*) And a waiting list I gather?

(*Professor Poole*) And a waiting list.

185. Biotechnology is thought to offer some risks to health and the environment, what risks do you see?

(*Dr Dart*) I must stress at the outset that all the risks are perceived, in 20 years of operation of this technology there is no known risk that has developed as a result of the technology. I would break this into several categories. There are risks associated with the worry about creating the dangerous pathogen from something that was not a pathogen to start with and that is why the containment regulations are there. I was involved in some of the early debates in this and I can remember an experiment that Professor Ken Murray did because at the time they were thinking what is the most dangerous experiment we can conceive of and let us test it under high containment conditions. What they conceived of was inserting genes that caused cancer into a Mouse via the *bacterium E.coli.* These were the polyoma virus genes. So they put the genes into *E.coli*, fed the *E.coli* to mice, and asked whether the mice developed a polyoma derived tumour. The answer was no, in fact it was a safer way to look at and examine these genes, putting them into *E.coli*, rather than handling them separately. The mice did not get cancer. In fact, you could not even pick up any live genetically modified *E.coli* in the stools of those animals. That was one of the first indications that most of the laboratory organisms that people are working with are either disabled or incapable of competing in the wild. That is not to say that there will be some risks in some organisms. That is why the Advisory Committee on Genetic Manipulation exists, to monitor experiments. Nonetheless, this was one of the early concerns and explains why laboratory containment should be appropriate to the nature of the perceived risk. In fact, risk categories have changed as people have got more confident of what is potentially a risk and what is not.

Lord Perry of Walton

186. That in itself is an example of what is called horizontal regulation. There is nothing wrong with horizontal regulation at the laboratory stage.

(*Dr Dart*) Exactly, I totally agree. If I can move on to other risks in my sector. One that is always expressed as a concern is the chance in a plant breeding programme of creating a weed species out of something that was not by the act of genetic manipulation. What people actually do not realise is that a plant breeder is selecting from massive populations of plants for a set of defined characters of which yield and quality are both important and we would naturally reject anything through this process. A character like weediness is very, very complicated genetically and to actually create weediness by introducing one or two genes is almost impossible. If I were a plant breeder, and in fact I am responsible for a lot of them, I would be quite offended by any implication that I could inadvertently create a weed.

[**Lord Perry of Walton** *Cont*]
Most of the things I am creating are incapable of competing with the wild species in the environment and are only capable of delivering the effects the farmer wants. Nonetheless, the sorts of checks and balances that we have in these guidelines will always pick those sorts of things up. Another question has been genetic stability: if we put these constructs into a plant will they be stable, is there something funny about Recombinant DNA that creates some instability in the wild? Again the answer is plant breeders are in the business of supplying stable genetics to the customer and they go through seven years of testing to make sure that they are genetically stable. That has nothing to do with regulations, that is to do with the fact that they are selling seeds to the customer and if that seed is not stable they will lose the business.

Chairman

187. Do you not see it as a very risky business?
(*Dr Dart*) No, I do not see those sorts of things as a risky business but there are some that are actually implying that they are and I do not think they have the background of what goes on in those industries now to look at them.

188. Do you think the existing regulations offer sufficient protection against any—
(*Dr Dart*) Yes, I do. Yes I do, very much so.

Lord Perry of Walton

189. Can I ask another question? You have mentioned in passing two different, to me they seem very different, kinds of product, one is a viable GMO and the other is a non-viable protein or other pure chemical that can be released. Is there a reason for rewriting the regulations to cover these two things in different ways?
(*Dr Dart*) I do not think so. I think you need to deal with it more about perceived risk than viability of the GMO. Let me give you an example of something that we have been wrestling with in this horizontal/vertical debate. We are interested in producing improved tomatoes in various ways. I have been quite fascinated by some of the debates going on in this area. Most of what we are doing through Recombinant DNA technology could be achieved through the traditional breeding techniques but it would take longer. For example, you see on the shelves now yellow tomatoes, nobody buys them and it is no big deal commercially but those yellow tomatoes have been selected by standard natural selection procedures. That is a mutation in the tomato that stops it at yellow. Through recombinant technology we can create the same effect, exactly the same effect more efficiently. So you say: "Well what is the difference there between using this technology in a more efficient way and something that could have been produced already?" They are both viable GMOs.

Lord Whaddon

190. Neither of them sell?
(*Dr Dart*) In that case neither of them sell but I can give you examples of others. I thought I would use that one, it illustrates something around already, I will give you another if you like?

Lord Perry of Walton

191. The worries of the public may be quite unnecessary but they are there.
(*Dr Dart*) Yes.

192. It seems to me the worries need not be there at all for the non viable products of GMO.
(*Dr Dart*) Yes.

193. Whereas you cannot really wipe the worries about viable GMOs out completely?
(*Dr Dart*) Yes.

194. It seems to me we would take a step further, would you agree, if we were to divide the two up that way?
(*Dr Dart*) That is one division but I think there is another division as well which is to do with of the viable ones which ones are we relaxed about and which ones are we concerned about?

195. Risk assessment?
(*Dr Dart*) Which is risk assessment. The USDA have done this brilliantly in my view, they have had experts look at six major crops and try to conceive of every risk scenario and decide whether these crops fall into a low or a high risk category. For example, corn and soya beans are going to be the basis of a very simple procedure.

Chairman

196. These regulations you believe offer adequate protection to the public, how do they affect your business? Do they restrain your competitiveness in any way?
(*Dr Dart*) I believe that the regulations derived from the current directives, they are a bit of a lead ball at our feet compared with what we see in other parts of the world.
(*Professor Poole*) I think the concern with the European approach is we have set directives in place which have to be implemented at the national level which makes the statement that genetic manipulation is by definition dangerous and needs to be regulated. It is a horizontal regulation which covers everything from the research phase to placing on the market. We are worried about this for three reasons. The first reason is, Dr Dart talked about producing the same product by two different techniques, now if one of those products is covered by horizontal legislation and the other is not, you are actually getting two standards. That is not in our interest and it is not in society's interest to have two standards. The answer we believe is as soon as you have done your transformation and you have started to develop and then market your product, you go into vertical legislation which exists for all products and the skills to handle the risks and the benefits are actually within that vertical legislation. So, for example, if it is a vaccine and you are concerned about shedding the vaccinia into the environment, the lead should come from the Department of Health, that is where the expertise lies. If it is a tomato it is the Ministry of Agriculture, Fisheries and Food. What we are seeing here is this confusion developing between horizontal and vertical not at the laboratory stage, not at the

[**Chairman** *Cont*]
research stage but at the stage of development and marketing. We are worried about this duplication of standards. Another problem is that it is actually diluting effort. We are having to put in sometimes two dossiers to two different departments. We are putting scarce resources, and the Government resources as well, on to low prioirty areas rather than those that would require more scrutiny. I think also we are seeing increasing dissatisfaction or confusion about the role of vertical regulation, not just the GMOs but the non GMOs as well. Already in Brussels we understand they are writing new directives and new regulations to cover transport, to cover marketing of all genetically modified animals, to cover marketing of genetically modified plants, to cover pharmaceuticals, to cover patents. Only in Europe do we see this job creation scheme going on. The danger of it is it is affecting the whole regulatory system in Europe. Our system depends on trust by ourselves and by the regulators and by the public.

Lord Flowers

197. Is Professor Poole saying it is the bureaucratic rather than the technological aspects of regulation as having to be practised by you at present that causes you the greatest concern?

(*Professor Poole*) It is the over-bureaucracy, Lord Flowers, yes.

Lord Soulsby of Swaffham Prior

198. You mentioned the word trust on the part of the public but I would like to go back briefly to this question of competition between what we might call the wild or the normal plant and the genetically modified. While one might accept the competition on the one to one basis would be very much in favour of the wild plant, might there be a quantitative situation here that if the natural is overwhelmed by the genetically modified that the genetically modified might take over.

(*Professor Poole*) Yes.

199. I think that is the sort of worry the public might have, not that they do not believe you but they do not believe you can see far enough ahead in terms of quantitative situations.

(*Dr Dart*) I appreciate that is a public concern and one problem we have is trying to get the public to have a feel for what crop plants are like in competitiveness. There was an experiment I recall done I forget how many decades ago at Rothamptstead where they planted a field of wheat and they said: "Let us let it go fallow now and see, it might be 15 years time but let us have a look and see what happens to it". It finished up as a wood and there was no detectable wheat. What that is telling us is that the crops bred by man do not have the capability of competing with wild populations. If you add to that the fact you are putting one or two genes into this crop to create the disease resistance or whatever, how are those going to change the competitiveness of those plants so they can outstrip the woods? I find it very difficult to foresee how that would happen but that is what the regulatory authority should be there for. It is saying: "Okay you have put in the genes for resistance to a fungus or something, does that change its competitiveness or does it not?" That is something plant breeders can test for anyway and they have got many years to test for it anyway. I think that is a reassuring check at the end of a lengthy process.

Lord Perry of Walton

200. Can I come back to what Lord Flowers was saying about bureaucracy. There is a lot of talk in the submissions we get about the interpretation of the regulations and how it can vary. Does bureaucracy mean they are being interpreted wrongly or not sufficiently simply? Could they be interpreted in a different way by the British regulatory authorities so they became an acceptable and an easy way of handling it?

(*Dr Dart*) My answer to that, I think, Lord Perry would be yes. If I look at the US system which I was referring to earlier they have already decided that there are some crops which present minimal hazard and will require a notification procedure. We have just heard this morning it is going to be two pages and 30 days' notice to do experiments in those crops because they have been through the debate about the risks there. I would hope in Europe we move to some system that is like that where for some areas of low perceived risk we move to simplify procedures.

201. That would be presumably within the regulations as they exist without amendment?

(*Dr Dart*) That is a good question. We are certainly hearing the regulatory people telling us that is a possibility but we have yet to see it in action.

Lord Renwick

202. You do find good communication with the regulators and you do find that they are not written in stone, you do find they do think as the technology develops and knowledge of technology and the implications of the technology that the regulations could be changed to the favour of the competitiveness of the industry?

(*Dr Dart*) I think at the moment the dialogue with the regulators in the United Kingdom has been very good. I think our concern is how that dialogue gets translated into Brussels and whether Brussels will really listen.

Lord Flowers

203. Can I ask a slightly different question: in order to get some sort of measure of how burdensome you find biotechnology regulation, you are regulated in all sorts of other ways? You are audited, for example, you have ordinary health and safety regulations, innumerable things, regrettably perhaps, how burdensome is biotechnology regulation?

(*Dr Dart*) That is a difficult question because it is a bit apples and oranges, if you like. You know in the health care area the regulations and development of a drug are massively expensive and if that happened in my sector it would just totally render that sector uneconomic and also it would not be balanced with the perceived risk in my view. So compared with things like that, you would have to say these regulations are not onerous. You have got to look at it within the costs of the sector you are dealing with and the risks within that sector.

Lord Perry of Walton

204. If you take one of your medical proteins, will that not have to go through the Safety of Drugs Committee after it has gone through these regulations?

(*Dr Dart*) Yes. That is your horizontal and your vertical.

205. That would be a duplication?

(*Dr Dart*) Yes.

206. Would you argue that you want to cut out the GMO regulations and go for the Safety of Drugs' regulations?

(*Dr Dart*) Yes. My argument would be, as I think you said earlier, at the laboratory phase there is no problem about horizontal regulations. There is a stage when you move into development and marketing when it ought to go down the track where the most competent people can judge whether it should be marketed. I would say in the drug area it is the Safety of Medicines and in the agricultural area it is MAFF. MAFF look after pesticides now and they also look after the registration of plants.

207. The reason I asked the question about viable and non-viable is that in the drug area we normally are thinking of the non-viable . There may be an occasional viable application to man although I do not know them yet.

(*Dr Dart*) Yes.

208. In that case it might not fit into the Safety of Drugs' regulations. That was the reason for my question.

(*Dr Dart*) I see, yes.

Lord Whaddon

209. There are large parts of the world where there are no regulations at all at the moment. Have you any knowledge of any research emigrating to those areas and are there any risks that you know of due to the fact that there are areas of the world with no regulations? If so, what do you do about it?

(*Dr Dart*) If I can start and perhaps then pass it on to Nigel. We have had this problem already because we wanted to do a bulk up of genetically modified tomato seeds in Chile, in a winter nursery sense to bulk up for the next summer in America. The problem we faced was that Chile did not have any regulations. What we decided as a policy was to apply the same regulations to ourselves in Chile as we would in the United Kingdom but we would talk to the agricultural ministry in Chile, tell them what we were doing and ask their permission. Also there is a gentleman based in Costa Rica, a professor there, who takes upon himself a sort of overview of Latin America in this area so we consulted him as well. We have had to go through those sorts of things in that country.

Chairman

210. If you are working in Chile with a view to the American market why did you apply United Kingdom regulations and not American ones?

(*Professor Poole*) There are two reasons for that. First of all we are a British headquartered company. We have a very strong ethical position. For agronomic reasons we have to work in areas which do not have a regulatory framework so we set ourselves the British standard. As the experiment was also going on in America we ran it through the American system as well, so we did it twice. We translated the whole lot into Spanish and walked around every single agency we could find in the Chile Government and local government and explained what we were doing. We do not want to do, and will not do, experiments in third world countries, because they have no regulations.

Lord Whaddon

211. There are a number of countries which are well known for having zero regulations. Do you not find undesirable competition or unfair competition?

(*Dr Dart*) Most of those countries are not competing with us in our market in the seeds business. In a competitive sense it is not a concern. I think in the sense of harmonising guidelines and making sure that we are all progressing in a safe way that is a concern. I know the OECD are trying to get guidelines that will apply to all the countries in their purview.

212. Is there any particular hazard you have in mind?

(*Dr Dart*) No, I am just speaking in general terms.

Chairman

213. Can you tell me whether the existence of these regulations imposes any burdens on your business strategy rather than scientifically?

(*Dr Dart*) For ourselves at the moment, no. I can see for some people it might provide the wrong sort of climate of business confidence. We are concerned, for example, by what is happening in Germany because Germany for us is a major market for most of our products. I am sure your Lordships know that there are problems in Germany with Hoechst in their insulin plant and the fact that Behringer Werke have decided to put their GCSF plant into America. That sort of thing does give us concern. Partly the regulations are affecting public perception in Germany and if that climate spreads then certainly it will affect our business developments.

Lord Flowers

214. May I ask is that peculiar to biotechnology or are there other industries you know of where people are moving to the States or elsewhere because the regulations suit them better?

(*Dr Dart*) I cannot think of any.

(*Professor Poole*) I do not really know.

Lord Perry of Walton] Animal experimentation might be the same sort of thing.

Lord Soulsby of Swaffham Prior] There is a lot of this today with animal experimentation. In fact, in Switzerland many of the major pharmaceutical companies are moving out because biotechnology involves animals, some to Germany.

Chairman

215. We have got to the stage where the Committee answers its own questions! That is very useful to all of us.

[**Chairman** *Cont*]

(*Professor Poole*) The major problem industry faces is one of confidence and trust in the attitude of the European Community and where we in Europe are going. Decisions then have to be made about where to do field trials. As I said, the Clinton administration yesterday approved their notification system. Already it costs a lot more to do the experiment in the United Kingdom than in the US so it will be even easier to do experiments in the US than in the United Kingdom. I would add on that I do not see any evidence that the US system is any riskier or any more dangerous. I think this is one of the problems we face, the belief that additional regulations, additional bureaucracy, actually increases safety. It does not, it is the appropriate level of safety regulation which guarantees it.

Lord Perry of Walton

216. Is the easing in the States due to the fact that they have a longer and bigger experience? Is this not likely to happen here as well?

(*Professor Poole*) America is one of the countries you look at as being grossly over-regulated, wherever you go you see signs telling you not to do this, or that. Do not look over this cliff in case you fall down, it is that sort of culture. In this sort of area what the Americans did, and I think we can learn from them, is first of all they had considerable public debate on biotechnology, they looked at the benefits for the American society and they looked at the risks. Then under the Bush administration they produced a number of policy papers which identified the policy. There was considerable debate, not just among the scientific community but with the legislators, the public, all sectors of society, and they agreed their policy after debate. They then put a regulatory framework in place. They have done it in such a way, because they have had special legislation, which allows them to increase or decrease the amount of regulatory oversight as experience is gained. The Clinton administration, as of yesterday, has approved the USDA policy with one minor modification which industry answered for them.

Chairman

217. On the EC Directives we were told, I think by the Health and Safety Executive, that in due course technical amendments can be made to these Directives. Are you presenting your views to the Government and possibly to Brussels with a view to influencing any changes in these Directives?

(*Dr Dart*) Yes we are, through every available channel, certainly through SAGB and certainly through our contacts with the regulators in this country. Indeed, one of the big flaws in my area in the Directives was its lack of appreciation of plant breeding and the plant breeding process and the definition of plant breeding. We had a long discussion over 14 months ago with the DoE expressing our concerns in relation to those definitions. As a result of that I think we convinced our DoE colleagues there was a problem which they have then taken to Brussels for debate there and some re-interpretation of those definitions. So it seems as if there is some re-interpretation possible within the directive but clearly the directive itself is flawed and needs re-visiting at some time in the future but we are told that is a fairly lengthy process.

Lord Perry of Walton

218. On page 6 in the paragraph you say: "Simply transferring the requirements of Directive 90/220 into vertical regulation may be an administrative solution, but we fear that this will be a case of 'building a house upon the sand'." Why? Why should that be? If they are transformed into a vertical regulation it would seem to me it could solve the problem?

(*Dr Dart*) Yes, I think we were referring to the combination of horizontal and vertical and the confusion that would create.

(*Professor Poole*) We were trying to put some feeling into the document. Just moving, for example, annex 2 of Directive 90/220 into for example the pharmaceutical legislation or into the food legislation or into the pesticide legislation is administratively nice but you are actually just transferring the problem from one regulatory track to another. You are still saying a GMO should be regulated differently, because it is a GMO. What you should be saying is: "This is a product to achieve an effect, I wish to examine the risk of that product". The fact it may be genetically manipulated as part of that investigation is not the sole driving force. I want to look at the product safety and then I bring in the fact it is genetically manipulated as part of that. Moving regulations over makes life easier but we wait to be convinced. Our legal advice, the advice of my colleagues, and experience has taught us that such a move is risky but it might be all we can do.

Lord Renwick

219. Professor Poole, it seems to me Zeneca as a commercial organisation will impose its own regulations, it will impose its own tests to make quite sure that the products that are produced are saleable and resaleable and stand the test of time and are competitive.

(*Professor Poole*) That is right.

220. What we are really talking about is are the regulations imposed either by Europe or by the United Kingdom anything really dramatically—in which section—more onerous on the company than you would impose yourselves for humanitarian and as regards the long term commercial considerations?

(*Professor Poole*) First of all, yes, we insist our review is a more strict review than anybody else can apply for us because as you said the name of my company is more important than anything. Secondly, as examples where we feel perhaps we are not prioritising our resources correctly would be Annex 2, of 220. 89 questions have to be asked and filled in. If I am examining releasing a crop plant, a wheat or maize plant in this country a lot of those questions are not relevant to the release but we still have to fill them in and explain why they are not relevant. If you wish to suggest an improvement you would take Annex 2 and say: "These are generic questions and these are questions which have to be answered for bacteria, those for a virus, those for a plant, those for animal", there is a much more

[**Lord Renwick** *Cont*]
streamlined procedure which is what we are looking for.

221. It does seem there is quite a big learning curve up which the regulators have yet to go rather like me.
(*Professor Poole*) We are all learning together.
Chairman] I am glad to hear you are going up rather than down!
Lord Renwick] Certainly recognise it is there.

Chairman

222. One of the DoE witnesses told us that the differentiation between horizontal and vertical regulations was academic, if the regulations are risk based. Do you agree with that?
(*Dr Dart*) Not at all. If I can use another example which I promised to give you earlier. We are selling a herbicide resistant corn in the States, herbicide resistant maize which is in fact resistant to a competitor's herbicide but we sell it because we believe it gives the farmer a benefit for treating some weeds. We have produced that using a traditional technique not using Recombinant DNA at all. We could have done the same experiment using Recombinant DNA. Our argument would be that in order to judge the safety of this material you look at the product. You say: "Is this herbicide resistant corn plant something that is okay in the environment and is going to be genetically stable and all those good things?" and not "Have you produced it by Recombinant DNA or have you not?" That is one of our first living real marketed examples. As it happens what we did with our product was we went to the USDA and told them what we had done for their information. We involved the local university agricultural extension services to tell them what the product was about and give them the right background and we did that in case of misinterpretation but also because this was a new product in the corn belt. It was the first product out there with this particular characteristic. That is looking at the product not looking at the way you make it.

Baroness Hilton of Eggardon

223. One of the problems it seems to me about looking at the product is that is the way you might excite public anxiety. Is this not what has happened over tomatoes in America that because you are actually looking at licensing the product people become unduly concerned about the particular product whereas in some way looking at the horizontal process may be too obscure perhaps for the public to grasp and you might not get the same sort of public panic about that particular product.
(*Professor Poole*) I think that is an interesting point, Lady Hilton. I think the answer to that is one of your own values. We wish to put a product on the market which is safe. Vertical regulation even though it is looking at products is the way we guarantee that safety. We have to live with those values, that is the best guarantee we can give of safety and that is what we are concerned with here.

224. In doing that you may in fact alarm the public more than by the horizontal process.
(*Dr Dart*) I do not understand why.

225. Because to them tomatoes are familiar or more than familiar or whatever so if you are actually looking at licensing a particular product that may grab the public's imagination whereas they are not familiar with scientific horizontal processes. You may not have a Frankenstein's monster on the ground, you are not going to alarm the public so much by just looking at that process.
(*Dr Dart*) I can understand that the public could get alarmed by somebody like Jeremy Rifkind telling them: "This is the thin end of the wedge"—

226. And holding a tomato in his hand.
(*Dr Dart*) Yes, and holding a tomato in his hand. We have to do a lot to make sure the public understand how this tomato has been created and how it relates—

227. You are looking at the processes again?
(*Dr Dart*) Yes.

Lord Flowers

228. Chairman, I am still grappling with bureaucracy, if I may.
(*Professor Poole*) Are we not all.

229. You have to answer a very large number of questions, 89, are they imposed by DoE or by Brussels and which is the harder taskmaster?
(*Professor Poole*) The 89 questions came from an OECD report in 1986 perhaps as suggestions for how to evaluate things. That report, which is actually very interesting, also made a point there was no scientific justification whatsoever for the regulation of Recombinant DNA because they are recombinant. Those questions were then taken up and put in Annex 2 of 90/220 which is a directive and which as part of Europe has to be applied in this country. Those questions, therefore, came from Brussels, not just Brussels, but from the European Community and we have to answer them under national law.

230. Who supervises your implementation of them?
(*Professor Poole*) The Department.

231. Presumably the Department?
(*Professor Poole*) Yes.

232. So the extent of the bureaucracy which you suffer, if I may use that word, is insisted upon by the DoE on behalf of Brussels?
(*Dr Dart*) To be fair to them they may say this is part of law.
Lord Flowers] What I was really going to ask next is if it emanates from Brussels then how does what DoE do to you compare to what corresponding ministers in similar countries do to their companies?

Chairman

233. I think I can add to that question by saying we are told that the Directives, the regulations and so on, are intended to provide what is nowadays called the level playing field, is the playing field level is the question?
(*Dr Dart*) Our impression is that the interpretation in other countries is somewhat different.
Chairman] I think we are running out of time, unless you are absolutely sure you must ask this question, and I am sure you are.

Lord Perry of Walton

234. Obviously ICI and Zeneca are very competent, but do you think with the growth of the subject and the money involved that new companies could spring up and pay less attention than you do to the quality of safety and if regulations are made simpler for you would they be made too simple for them?

(*Professor Poole*) The answer to that is the importance of inspection. One of the things we do support is competent inspections and we welcome that because it improves our performance and guards against the areas you were saying.

Chairman] We will have to draw to a close there. There may be further things you would like to let us have amplifying your evidence or adding to it and we would be very pleased to hear anything from you of that kind. Thank you very much.

Written Evidence from Glaxo Group Research Ltd

1. *The Glaxo interest in Biotechnology*

Glaxo is involved exclusively in the discovery, development, manufacture and marketing of prescription medicines for the treatment of human diseases. Our drug discovery and development activities are based upon the application of science and technology to understanding disease mechanisms, and from this the discovery and development of novel medicines. Biotechnology is regarded by us as essential to these activities.

Glaxo has been engaged in "biotechnology" in the form of fermentation technology for many years and this is important for our production of penicillins and cephalosporins used in the treatment of infectious diseases. Fermentation is used elsewhere in the industry in processes leading to the production of medicines such as the immunosuppressant cyclosporin, and was initially used in the discovery and isolation of the cholesterol lowering agent mevinolin. Although fermentation technology may be regarded as "old", it is still undergoing development within the pharmaceutical and chemical industries as it affords a means of using micro-organisms in the synthesis of molecules which cannot easily be made by conventional chemistry—ie by biotransformation. It should not be overlooked, therefore, in any consideration of the role of biotechnology in industry.

The more usual meaning of "biotechnology" now embraces the developments which arise out of the application of genetic engineering. It will thus cover many applications of modern molecular biology and chemistry employed in the field of gene cloning, expression of specific proteins by cells and organisms in culture, the production of transgenic animals, "gene therapy", protein biochemistry and protein structural chemistry. Glaxo does not, at present, have any proteins derived from the application of biotechnology in development as potential drug candidates. Other companies in the pharmaceutical and biotechnology industries have developed such proteins—eg erythropoeitin, interferons and interleukin-2.

Genetic engineering is used extensively throughout Glaxo Group Research for many purposes. For example, we use biotechnology as a means of providing pure proteins, such as enzymes and receptors, and modified organisms, such as yeast and bacteria, as tools in the process of drug discovery. These "tools", when applied to other disciplines such as cell biology, biochemistry and pharmacology, provide us with potential therapeutic targets and screening systems. The use of transgenic animals is being explored by us as a means of understanding disease processs and may also provide convenient animal models for human disease in which candidate compounds can be evaluated prior to entering the development process. In the case of a number of important diseases requiring new methods of treatment, animal models do not at present exist. Genetically modified organisms are also used for the resolution of racemic mixtures of compounds and the improvement of titres of natural products.

2. *How and why is Biotechnology important to UK industry?*

It is important to realise that the term "industry" covers a wide range of activities which should have the potential for wealth creation in the UK. Each sector will have its own particular problems, needs and solutions. The application of biotechnology has the potential to make a very significant contribution to the future economic success of the UK manufacturing base. Glaxo's activities are exclusively in the area of discovery, development and marketing of prescription medicines and it is only from this position we can comment upon the importance of the development and exploitation of biotechnology.

From the perspective of the UK pharmaceutical industry the understanding of the molecular basis of human diseases is essential to drug discovery research. Biotechnology is being applied to help in this understanding and the identification of target molecules at which new medicines can be aimed to provide effective specific and safe treatments. The industry in the UK has been highly successful. As evidence of this it may be pointed out that at present six of the top twenty prescription medicines in use in the world are UK discoveries. We see the application of genetics, molecular biology and biotechnology as essential for the industry if we are to be able to maintain this record of achievement.

The applications mentioned above are merely examples of the value of biotechnology in the pharmaceutical industry. They, and many other applications, will be seen to have application for other industries engaged in a wide range of activities ranging from sewage disposal to agrochemicals. Adoption of these techniques is essential if UK industry is to remain competitive and indeed UK industry should lead in the adoption of these techniques, if it is to become a world leader.

3. *What future prospects and opportunities does the technology offer?*

We believe, for reasons given above, that biotechnology has enormous potential in improving human healthcare. The human genome mapping and sequencing initiatives at present underway offer the prospect of understanding all hereditary information and understanding the genetic basis of diseases. This new knowledge will have an impact upon drug discovery in a number of ways but, in particular, will allow the identification of new points of intervention in a number of important diseases. Already we are seeing novel therapies being tested in inherited disorders, such as cystic fibrosis, and new drugs with decreased side-effect profiles. Both developments owe their existence to information provided by genetic engineering. The opportunities for reducing human suffering by exploiting developments in biotechnology to discover new medicines is now enormous.

In other areas, we can expect to see better food crops and cleaner manufacturing processes.

4. *Which developments in Biotechnology raise issues of safety and how should they be addressed?*

There is a widespread popular impression that all genetic engineering is dangerous and the products of the technology represent an environmental and/or health risk. This is clearly wrong. Legislation on safety which panders to this view is not useful and is likely to be ignored by many who see it as illogical.

'Genetic engineering' has gone on for centuries in the form of selective breeding programmes and many of the domestic animals and food crops we have today are products of this. Nonetheless, the new technology does offer the opportunity to mix the DNA from species which could never have been mixed by traditional techniques. Thus, it is not difficult to see that toxin genes could be introduced into normal human commensals such as *E.coli*. Clearly such organisms would be dangerous and should not be made without adequate containment and other precautions.

Most of the safety issues surrounding biotechnology, such as deliberate release and contained use, have been covered by existing legislation but the situation is not entirely satisfactory. We believe that there is too little interpretation of EC Directives so that they fit with the local situation and there is, rather, the desire to alter the local situation so that they fit with the letter of the EC Directives. It must also be noted that anyone deliberately setting out to make a dangerous organism, for any reason other than legitimate research, might not feel constrained by existing legislation. The current legislation thus runs the risk that it could unduly restrict legitimate and largely safe experimental work whilst making no provision for dealing with those who set out to mis-use the technology.

The ethical considerations of those aspects of genetics relevant to our industry and human medicine and their implications, particularly with regard to the rapidly developing use of gene therapy, are adequately addressed by the Clothier Report.

A further consideration of importance in the context of legislation and regulation is the likely effect upon industrial competitiveness. We suggest that an excessive bureaucracy in this, and other fields, will have a detrimental effect on competitiveness.

5. *Should Biotechnology be regulated by an industry-specific regime?*

We believe that there is every reason for industry to be encouraged to regulate itself in respect of its use of biotechnology, and of the products thereof, rather than be dictated to. We do not consider that there is any good reason why biotechnology should be regulated in an industry-specific manner because biotechnology research in industry uses precisely the same techniques as biotechnology research within academia and should thus be regulated in the same way.

Legal requirements of the Health and Safety at Work legislation impose responsibilities which are such that industrial organisations must be responsible for the safety of their own staff and environment. Over the years that such regulatory requirements have been in force, industry has gained considerable knowledge of the safety issues in question.

The quality of biotechnology products in the pharmaceutical field are, like other medicinal products, subject to regulatory control by means of guidelines such as the "Notice for Applicants" and the requirements imposed by directives for "Good Laboratory Practice (GLP)", "Good Clinical Practice (GCP)" and "Good Manufacturing Practice (GMP)".

These safety and regulatory requirements adequately cover any differences between industry and academia.

6. *Where products are concerned is horizontal regulation better than vertical regulation?*

Horizontal regulation implies the judgement of the safety of a product through the process involved in its production whilst vertical regulation is concerned with the characteristics of the product itself.

In the pharmaceutical industry our products are regulated in a manner that does not recognise these two distinct modes. Thus the characteristics of the product with regard to both safety in use and clinical efficacy are addressed, but in addition the production process is also subjected to auditing and regulatory control through such directives as those regulating GLP, which is relevant to the development stage of an entity and GMP. The predevelopment phases of drug discovery research are not regulated by GLP and any attempt to introduce such regulation at this stage will have a serious and detrimental effect upon the creative processes involved in successful drug discovery.

As far as Glaxo is concerned, we do not have any products originating directly from biotechnology. This is likely to be true also for many other companies in the industry. Our use of biotechnology is, as has been outlined above, as a provider of "tools" and is concerned with the discovery of novel medicines. The final products emerging from these activities will usually be molecules derived ultimately from medicinal chemistry. We thus believe that there should be little horizontal regulation of the process because, if it were applied in our context, it would involve probing in areas of little direct concern to the final product and such regulation would be counterproductive. For example, if carried to an extreme, the development of drug discovery screens would be covered although they will be of no relevance to the final product's characteristics.

We believe that ultimately it is, in general, the characteristics of the compound itself which are more important than the processes by which it is derived. They are however clearly related, for example the process of production is relevant *vis-a-vis* expected or potential contaminants, but the current regulatory requirements address both issues adequately. During the process of product approval products derived by the use of biotechnology are subject to guidelines over and above those now applied to new medicines. Further regulation should be resisted unless such measures are clearly required.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

We believe that it should for reasons already stated above.

8. *How do current Regulations compare with those of other competitor countries?*

In Europe the regulatory climate is very variable between countries, even within the EC. The EC Directive in this area has unfortunately not yet been given effect by legislation in all EC member countries. Furthermore, there is considerable variation in the interpretation of this legislation throughout Europe. For example the interpretation has been very strict in countries such as Germany and Denmark, but as yet in Italy there is an absence of legislation as yet.

In the United Kingdom "The Genetically Modified Organisms (Contained Use) Regulations 1992" and "The Genetically Modified Organisms (Deliberate Release) Regulations 1992" were created in response to the EC Directive. We believe that in general the UK has adopted a more sensible approach to the issues than many other countries in Europe but there is evidence of a less than consistent attitude between Government Departments and Agencies. For example the HSE appears to have adapted a good intermediate position whilst the Department of the Environment appears to be far more rigid and less helpful.

The situation in the United States of America is much less bureaucratic and more enlightened. The starting position arises from the general assumption that most genetic engineering results in benign organisms rather than the assumption that genetic engineering is dangerous and should be minimised. Experience over the last twenty years has does not support this general position as there has been a lack of incidents involving genetically modified organisms during this period.

We have no knowlege of the situation in Japan and the Far East. However, it is our expectation that Japan would follow the lead of the USA.

We suggest that the key to sensible and successful regulation in the field of biotechnology lies in Governments taking advice from experts, drawn from both industry and academia, with the right knowledge and experience of relevant areas of science when formulating polices in this area.

9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of UK industry?*

The pharmaceutical market is a global market and to remain competitive the industry must seek to carry out its drug discovery and development activities in those environments which are most encouraging and amenable to progress in a rapidly evolving area. Thus excessive regulation will be detrimental to all aspects

of our business from the research activities to the market. If regulatory measures in any country place unreasonable restrictions on this work the result will inevitably be a transfer of activities to more sympathetic regimes.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK Science Base?*

We are assuming that the term "Science Base" in the question refers to those scientific and technological activities that take place within public sector institutions such as the Higher Education Institutions (HEIs) and Research Institutes. It is our view that there is not this danger at the present time, however there is a risk of this happening in the future. We are more concerned at the present time however with the serious decline in the HEIs and Research Industries and the possibility that there may be no UK public sector science base for UK industry to exploit.

11. *How best can issues of public acceptance be addressed?*

There is considerable ignorance about genetic engineering in both the public and the media. There is a tendency for the media to pick up and emphasise the negative aspects of biotechnology, that is the risks, rather than referring to the benefits that have already accrued from the technology and the potential benefits for the future.

It must however be admitted, that scientists working in the field are reluctant to explain their work in ways which are easily understood. This tendency creates an atmosphere of suspicion in the mind of the public and this can translate into antagonism. Biotechnology must be projected as a positive contribution to the health and welfare of society and issues of concern openly discussed. More contact between researchers and the media and public should thus be encouraged. An improvement in the quality of scientific journalism would be a major advance.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK Biotechnology industry?*

We believe that it is essential that the public sector science base in the UK is adequately supported in order that biotechnology, and other important areas of biological and chemical sciences are advanced in the UK. A healthy science base must be regarded as essential for the long term competitiveness of UK industry.

The UK Biotechnology industry, which could be a major contributor to our industry, requires better financial support than it is at present experiencing. The industry is at a disadvantage when compared with the better developed biotechnology industry in the USA. In the UK the venture capital view of biotechnology is short term and this situation is not helped by the British taxation situation and the UK Stock Market Rules. The result of this is that much good British academic science is not being exploited or, as has happened, is being exploited in other countries and in particular in the USA where UK academics find a more sympathetic reception for their inventions and ideas.

SUMMARY

1. Biotechnology in the form of fermentation technology has been widely used by Glaxo and other pharmaceutical companies for many years for the production of antibiotics and other important medicines. The "new biotechnology", which includes genetic engineering, offers considerable potential for the elucidation of the molecular basis of human diseases and the identification of novel targets for therapeutic intervention. It is regarded by Glaxo as a most important enabling technology for the discovery of molecules that may form the basis of new medicines for human diseases. We do not at present use biotechnology as means for the direct production of proteins and peptides as new therapeutic agents or vaccines although other companies in the biotechnology and pharmaceutical industries do.

2. Whilst it is important that we recognise the potential risks of biotechnology and the public sensitivities which surround the subject, it is important that the field does not become so regulated that progress is severely hampered or becomes impossible.

3. We believe that the current situation regarding regulation in the UK which has arisen in response to the requirements of the EC directive are broadly acceptable and will not seriously jeopardise the development and use of biotechnology in our industry. This is in contrast to the situation in other member States of the EC in which regulation is stringent and inhibitory or, at the other extreme, too lax. The USA, a major competitor in the biotechnology field, has a more enlightened view of regulation and is less bureaucratic than European regulations.

4. We believe that excessive regulation will be detrimental to our business and will reduce the competitiveness of UK industry.

5. The public perception of biotechnology, encouraged by the media, is a generally negative one and this does need to be changed. There is a need for scientists working in the biotechnology field to become more ready and open to discussing issues raised by the subject in the public mind.

6. Regulation is not the only threat to a healthy UK biotechnology development. Attention is also needed in the area of provision of financial resource for biotechnological innovation. In particular there needs to be a longer term view of the subject by venture capitalists, an encouraging taxation regime and a change in the Stock Market rules.

Examination of witnesses

DR J B WARD, Director of Microbiology and DR M WEIR, Head of Protein Biochemistry, called in and examined.

Chairman

235. Good morning. Thank you very much for coming to continue our education in this matter. I wonder if you would introduce yourself and your colleagues and if you wish to make a short statement on your general position in relation to biotechnology?

(*Dr Ward*) Certainly. I am Barrie Ward, I am the Director of Microbiology for Glaxo Group Research and I am accompanied today by Dr Malcolm Weir who is Head of our Protein Biochemistry Department. As you know Glaxo is one of the world's major pharmaceutical companies. We approach biotechnology in the sense of using it as an enabling technology. You are probably aware that we do not market biopharmaceuticals at the present time although clearly we do not eliminate this from future work of the company. As I said, we see biotechnology as an enabling technology which allows us to work in the discovery of new drugs. It provides a mechanism for us to obtain pure proteins, enzymes and receptors, particularly modified organisms as tools in drug discovery. Now we are starting to develop transgenic animals as potential models of human disease that will allow us to screen compounds more rapidly without actually having to go forward to man. I do not think we should underestimate our involvement in improving strains of micro-organisms for the production of natural products. Glaxo is one of the pioneers in terms of fermentation, old-style biotechnology. Whereas biotechnology in the public mind today has come to mean genetic manipulation and genetic engineering. I think also we should not forget the potential use of genetically modified organisms in the production of chiral compounds from racemic mixtures, that is the separation of mixtures of a compound that may be synthesized where one batch of that mixture's particular chemical structure carries with it the potential benefits and hopefully not the associated toxicities and in many instances enzymes can be used to separate those mixtures where chemistry would be extremely difficult. We have practice inhouse doing that and we use, or intend to use, genetically manipulated organisms where they provide benefit in terms of higher yeilds of specific enzymes, for example. Thus our underlying philosophy is as an enabling technology, but we do not rule out moving in the future into areas that we might define as biopharmaceutical.

(*Dr Weir*) I would like to underline the central nature of biotechnology for a great deal of the work we do now in the pharmaceutical industry and it should not be seen as a separate entity. 20 years ago there was no biotechnology, apart from fermentation technology going on in the pharmaceutical industry but now I think most of the techniques that form that technology are central to what we do in drug discovery from the identification of targets for therapeutic intervention through to the discovery of compounds and further developing of those compounds to get them into the clinic as medicines for major diseases. It is crucial to take that on board because it is essential technology and without it a modern pharmaceutical company could not survive.

236. As far as drugs are concerned, can you see a day coming when chemically produced drugs are largely replaced by biotechnologically produced drugs?

(*Dr Ward*) I think the simple answer is no. I see biotechnology and biopharmaceuticals as complementing the work of chemical drugs in the sense that there will clearly be some areas where biopharmaceuticals will be of benefit. Gene therapy may be a case in point where particular genes are constructed and then given to patients with a particular disease. I think there are many instances where it will complement but I cannot see in the future, at present, where they will actually replace.

237. But it might take quite a bit of the market, do you think?

(*Dr Ward*) I think it will take some of the market. When one defines "quite a bit", I think we are used to seeing in the press very large numbers quoted against biopharmaceuticals and I think with some of these we have to be very careful that those numbers have not been inflated because of reasons other rather than the actual market potential.

(*Dr Weir*) You have to think of it more in terms of creating new markets because new possibilities will arise which could not be addressed by the previous technologies. It will not be so much that you will replace aspirin with a protein, it is more a case of tackling some areas such as cancer or vaccine development where there is no good chemical way of tackling those problems and biopharmaceuticals, proteins, genes or whatever packaged in whatever way will enable us to treat diseases we could not otherwise treat. There will still be a great effort on making small molecule chemicals that interdict in biological processes because they have very good properties in terms of their synthesis and their transport into the body. The delivery basically is pills. There is a lot to be said for small molecules in terms of control of treatments.

[**Chairman** *Cont*]

238. Could you tell me is there any difference between natural insulin and GMO derived insulin?

(*Dr Weir*) The two different forms of insulin have actually been studied by x-ray crystallography which elucidates the atomic structure to a high resolution and there is no difference in those studies of the atomic structure of the insulin concerned. There is a difference in the initial use and treatment. There were some differences in how the diabetic patients responded to the different treatments and those have since, as I understand it, been put down to the greater levels of purity of recombinant insulin over the natural porcine-derived insulin and it is the change in the pharmaceutical regime. You get similar things happening when you switch to different types of drugs that act in the same way in traditional medicine.

239. So you are saying there is no scientific difference though there might be a difference in purity?

(*Dr Weir*) I think there is a scientific difference in that regard. There are two different questions. Are the molecules the same? And the second is are there other molecules in there the same or different? I do not have a deep understanding of this. Insulin is not anything we have been working on in Glaxo but, as I understand it, the difference is in the contaminants rather than any other problem to do with the insulin molecules.

Lord Perry of Walton

240. The molecules are different in purity.

(*Dr Weir*) In terms of the overall fold of the protein.

241. They are two different substances.

(*Dr Weir*) In that regard they are different, yes.

Chairman] Back again to answering your other question.

Lord Perry of Walton] I am sorry.

Chairman

242. No, no it is good I think. Let us think a bit about the regulatory system under which you work. Do the United Kingdom regulations affect your competitiveness as a company for good or ill?

(*Dr Ward*) I think at the present time the answer to that is that they do not but I think within the company there is concern that depending upon their interpretation then there is the possibility that they could affect our competitiveness.

243. But they have not so far?

(*Dr Ward*) They have not so far but we are in a situation where we do not yet know quite know how these new regulations are going to be interpreted.

244. Now to a large extent these regulations are for the protection of the public and so on. What risks do you see in biotechnology and do you think the regulations are effective in dealing with these risks?

(*Dr Ward*) I think we have to recognise that within biotechnology then there have to be a multiplicity of risks depending upon the system with which you are working. I think one of the problems that we have at present is the perception that just because it is genetic manipulation it provides an overall risk that requires very strict regulation. I think we have got to step back from that. Clearly if we were working with potential toxins or producing very pathogenic bacteria or viruses then we would need to adopt a certain regime for the use of this whereas in other cases, perhaps we were looking at a receptor or an enzyme that is fairly ubiquitous among mammalian species or even among bacterial species then the risk associated with work of that type I believe would be less. We are coming from a premise that all genetic manipulation is evil, if can put it that way, or has a very strong risk associated with it. I think I would prefer to argue that there are risks associated with it but we need to take this on a case by case basis. We have a long history in this country of very effective regulation of genetic manipulation which I think we should recognise.

245. Do you think it is satisfactory from the point of view of protecting the public?

(*Dr Ward*) I think there are a number of issues here. We must distinguish between laboratory research, which is really what we do now within Glaxo, through let us say drug development to commercialisation and at each stage risks will need to be assessed but in terms of laboratory research I think the way the Advisory Committee regulations have been handled in this country have been really very very successful and I do not think we should lose sight of that.

Lord Perry of Walton

246. All you are doing at the moment is in a contained sense. You are not marketing.

(*Dr Ward*) We are not marketing.

247. You are marketing pure chemicals.

(*Dr Ward*) We are marketing pure chemicals.

248. Am I right in thinking after doing your drug screening on the isolated receptors, GMOs, whatever it may be, that you make the new compound without any contact with the GMO at all? It presumably then becomes a scientific process which has nothing to do with the GMO at all?

(*Dr Weir*) Our whole business is geared around using GMOs and the way we use them has a great effect on what we do.

249. That is in the research field and development field but in the manufacturing field you move away from that?

(*Dr Ward*) There was a time, you are quite right, when Glaxo was involved in the vaccine business but that was at a time when genetic manipulation had not come into play. We have never been involved in that way.

250. What I am trying to get at if you find a new drug with your screening using GMOs it may be they have been manufactured in a wholly separate building where there is no GMO contact whatsoever in which case you are not, in my view, falling within the release side at all.

(*Dr Ward*) We are not falling within the release side; we are only working within the contained use side.

(*Dr Weir*) That is our understanding of the legislation. That is an issue of interpretation. That is how we interpret the EC Directive and GMO regulations on contained use and deliberate release.

Lord Soulsby of Swaffham Prior

251. Presumably, Lord Chairman, the fact that you are using this as an enabling technology means that you come under less criticism than you might do if you were producing genetically modified vaccines or organisms.

(*Dr Ward*) I think that is true at the present time. Within Glaxo there is certainly a degree of uncertainty as to how the contained use regulations are going to be interpreted. I guess that is what I am trying to get across to the Committee.

Chairman

252. Does that mean that the degree of uncertainty about the regulations determines to some extent your business strategy?

(*Dr Ward*) No, it has had no effect on our business strategy to date.

253. At all?

(*Dr Ward*) To date but clearly the interpretation of the regulations might. I think we have seen this within Europe where there has been a different degree of interpretation and the effect that has had on strategic decisions within other areas of the pharmaceutical industry. I think we have to recognise that we are working in a global industry and that in certain countries, for example, Germany—which I am sure we are all aware of—there the impact of regulations and the impact of pressure groups has caused a significant withdrawal from work of this kind.

254. Can you give us some examples of this?

(*Dr Ward*) The Hoechst insulin plant in Germany has never actually operated.

255. Are there others?

(*Dr Ward*) I believe there are others. In terms of information that we have heard with regard to other production pharmaceutical companies they have not developed there in the way that one might expect them to do.

256. Germany is particularly sensitive?

(*Dr Ward*) Germany is a particularly sensitive country, yes.

Lord Perry of Walton

257. I take it from the regulations there are two kinds of process in dealing with the laboratory side; one is getting consent in advance and the other is notification?

(*Dr Ward*) Yes.

258. Is a problem in dealing with isolated receptors and things of this sort the fact you worry about having to get consent? If you simply notified there would be no problem?

(*Dr Ward*) I think that is correct. In the past, as you are aware, in the Advisory Committee guidelines on genetic manipulation it was clear that we could take a certain view in-house and notify the HSE of the view that we had taken. Now we appear to be in a situation where we are going to have to seek consent before we can actually carry out the work.

Lord Whaddon

259. Some countries are notable for not imposing regulations—Italy has had a very relaxed view on medical regulations for as far back as one can think. Are you aware of any difficulties that are arising in Italy in this work due to a lack of regulation?

(*Dr Weir*) You mean instances of accidents or anything like that.

260. Yes, first of all. Secondly, do they gain any advantage over you for that which you have regulations and they do not?

(*Dr Weir*) I am not aware of any accidents that have occurred.

(*Dr Weir*) Not to my knowledge.

(*Dr Ward*) In terms of advantage I think again that is very very difficult to judge. Much of this work is not carried out in the public domain, so it is difficult to know what advantage they have got or not at the present time. I do not think we can answer the question.

261. Would you rather that they were regulated?

(*Dr Ward*) I would be much happier, to use the colloquial phrase, to see a level playing field.

Lord Renwick

262. We have heard before about levels of inspection. Obviously in the United Kingdom there are relevant levels of inspection, but do you think there are in other European countries, following on Lord Whaddon's question?

(*Dr Ward*) I can only comment in terms of our own operations which are in Switzerland and in Italy. As far as I am aware, there is no inspection in Italy. I have never heard any comment about any inspection having taken place there. The amount of genetic manipulation that we do in our laboratories is relatively small. In terms of the Glaxo Institute for Molecular Biology in Geneva, then I believe that they are inspected. They are certainly expected to work to the same standards that we work to within Glaxo.

263. Would you like to speculate on what risks might occur on totally uninspected activities if there were any cowboys in your profession, God forbid?

(*Dr Ward*) I see no reason to believe why our profession is any different from anybody else's. I am sure there are cowboys. Perhaps this is not the answer you are seeking, but I think if I can turn it round the other way and say, if the regulations and the inspection criteria are onerous then this puts a greater emphasis on cowboys perhaps taking the chance and doing things outside those regulations if they believe that they can get away with it.

264. For a short-term advantage only, because unless they impose their own strict regulations they might possibly produce an image-damaging product?

(*Dr Ward*) I think that is right. I think it is a balance, is it not? If they do not produce an image-damaging product then, in effect, they have got away with it.

Chairman

265. Did you say you have an operation in Italy?

(*Dr Ward*) Yes, we do.

266. Is it inspected?

[**Chairman** *Cont*]

(*Dr Ward*) Not as far as I am aware.

267. Is that the reason why it is in Italy?

(*Dr Ward*) No, it is not. I did point out the amount of genetic manipulation work we actually do there is very, very small.

268. We have heard quite a lot in the few weeks we have been undertaking this investigation about horizontal and vertical regulations. Have you any views on these? The DoE told us the difference between them was academic but others have told us that it is not. What do you think?

(*Dr Weir*) I think the key issue for regulation of a product is what actually ends up in the product. If, as is the case in traditional medicines, those regulations take into account how the product is made then that is sufficient in terms of regulation; because you can make a connection if you think a process may lead to some contaminant. For example, if you made a blood product from blood sourced in different countries that were prone to different transmittable diseases that may be blood-borne then you would consider those differently because of where they came from. In an ideal world you should be able to measure everything that is in the pot anyway, and you would not have to worry about those sorts of issues, but in practice they should be taken into account. I see no reason to regulate separately the process from the product. The processes are regulated. We have to do things in industry to good manufacturing practice, good microbiological practice, good laboratory practice, and to get products on the market we have to follow those rules. In essence I think that vertical regulation, as I understand it, would subsume horizontal regulation if it was done properly.

(*Dr Ward*) I think we have to clarify that we are talking here only in terms of medicines and biopharmaceuticals.

Lord Soulsby of Swaffham Prior

269. I am interested in your comment about good laboratory practice and the rest. While I accept what you say in terms of control and inspection should be sufficient, there have been one or two major compounds that have come out medicinal compounds that have got on to the market without these. They were not following the guidelines at all, and in fact were breaking the guidelines. This is in the United States, not mentioning the firms of course.

(*Dr Weir*) That would be a very serious thing, but I think with any guidelines or rules that you have that could happen if they were not properly prosecuted.

270. What is the safeguard now? I think the public are a lot more concerned about genetic modification and the gene. They perceive perhaps, quite wrongly, that these may do infinite harm. While the testing of a pharmaceutical product can be fraudulent, the public perceive that fraudulence in the genetic side is of much greater seriousness than just the chemical side.

(*Dr Weir*) I would see no grounds for that perception. I really would not. I think that at the end of the day if you are producing a protein therapeutic by recombinant means then you have a set of problems which are specific to that particular product and they need to be considered in that way.

271. In your case, yes, you are using this as an enabling technology, which is not always the case with biotechnology?

(*Dr Ward*) No, but I think with, say, a protein that is developed by genetic manipulation that people wish to market, if the same regulations apply that are currently applied to any other drug substance with the same rigour then I think the public is safeguarded. I accept what you say in terms of the current public perception in terms of genetic manipulation, and I think that is something we probably will address later on in terms of how this might be improved or how it might be manipulated. In a sense, I think we have to refer back to Lord Renwick's previous comments, in the sense that you can make the most rigid regulations but if people perceive that there is a major benefit to be obtained by ignoring them they will ignore them until they are caught. I think it is very, very difficult to legislate for those sorts of situations. I think, thank God, that they are relatively few and, of course, whenever they do happen that they achieve maximum publicity.

Chairman

272. Can you tell me, have you much experience of dealing with the regulations in the United States?

(*Dr Ward*) Yes. Malcolm in fact has spoken to our people in the Glaxo Research Institute prior to our coming here.

273. Is it an easier world there or more rigorous? Is it easier to deal with and less bureaucratic, for example?

(*Dr Weir*) Yes. As I understand it from discussions with the biological safety chairman in the Glaxo Research Institute, the amounts of paperwork involved, in growing, say, at a ten or 20 litre scale a recombinant organism, are negligible compared with what we have to do. It is much easier and there is a blanket cover and inspection of the site. There are National Institutes of Health guidelines which are voluntarily followed in the United States. The difference is mainly one of degree, I think. It is not a case that they are not regulated, they certainly are, and they do understand there are risks inherent in these processes, as is the case in any manipulation of a bio-active substance or a biological agent.

274. Do you think the United States' regulations give a similar degree of protection to what we have in this country?

(*Dr Weir*) That is my perception from discussions; it is not from firsthand experience.

275. Would you like to see the United States system applied here?

(*Dr Weir*) Yes, I would.

276. You would.

(*Dr Weir*) Yes, I think it would cut down our paperwork. It would not, in my opinion, entail any greater risk to either the public or to the health of my staff who have to do the work.

Chairman] One of the things I like about these two witnesses is they use words like yes and no at appropriate times!

Lord Renwick

277. May I ask, Dr Weir, what would be involved in making the change from US regulatory procedures to United Kingdom regulatory procedures?

(*Dr Weir*) I have mulled this over when I got the questions sent to me. I think one way of simplifying things and streamlining the regulations would be if we considered the handling of Genetically Manipulated Organisms in the same way we consider other health and safety issues and other environmental issues in the company, in other words if the GMO regulations were part of the ACD category, that is the Biological Agents Directive, part of COSHH I see no *prima facie* case for having separate regulations for GMOs. If we consider, for example, a process that does not involve any genetic manipulation, we consider the safety aspects component, aspects of the health of the public and the health of the people doing the work. These are major issues on concern to us.

Chairman

278. I wonder if I could ask you to let us have a brief paper comparing the United States and United Kingdom regulations?

(*Dr Weir*) Certainly.

Chairman] Giving your opinions on them by the way.

Lord Renwick

279. Before we leave this subject could I ask you whether you have put this to health and safety organisations and others and what was their response?

(*Dr Weir*) I have not actually put it to them because the recent EC Directive implementation has only just come through. One lives with regulations and I would not criticise the ACGM regulations unduly. We have got used to them. We know the system and we have only had to do retrospective notification. There has not been this issue of prior permissions to do work. It is still unclear to me and many of my colleagues to what extent the EC Directive and its implementation will actually affect in practice the work we do. I think there are many ambiguities surrounding it. We have not got clear yes and no messages from these documents because they are meant to be interpreted. I think it is common practice that will tell us whether these regulations are onerous or not.

Lord Whaddon

280. You have spoken very intelligently about the regulation of hazards. Do you take the view that there are any ethical problems in biotechnology, for instance with transgenic animals and chimaeras? If there are such problems how do you deal with them?

(*Dr Weir*) I think there are clearly ethical problems when it comes to genetic manipulation in human beings. These are massive ethical problems. Those are addressed in the Clothier report and really quite well addressed in that report. In terms of transgenic animals there are always ethical problems in these types of manipulation whenever one does work with animals. There are ethical considerations but again animal breeding and the selection of different traits in animals basically via environmental pressure on the genetic make up of those animals is a time-honoured thing to do and I would not necessarily see those ethical problems as being insurmountable.

281. But the present regulations do not deal with that, do they?

(*Dr Weir*) I think the animal regulations do because the prime consideration in the ethics of the experiments you are doing and the suffering it causes to the animal, is whether that suffering is justified, if there is any suffering, by the experiments you are proposing? They are very strictly regulated and properly regulated by the Home Office.

(*Dr Ward*) I certainly support Malcolm in that. The way the Home Office regulations in terms of animal experimentation are conducted in this country are to a very very high standard and we have frequent dealings with the Home Office Inspectorate and the issues are addressed with them as we proceed.

282. Yes, I agree but this of course is not an EC regulation?

(*Dr Ward*) No, it is not, that is right.

Lord Perry of Walton

283. You say in paragraph 11, "Biotechnology must be projected as a positive contribution to the health and welfare of society and issues of concern openly discussed." I agree wholly. Do you consider it is the responsibility of the industry to permit this and pay for it or do you think it is purely a matter for government?

(*Dr Ward*) No, I think this has to be a partnership—I really do believe that. I think it is one of the major issues that we have to address in this country at the present time. Since we are specifically talking about the United Kingdom—although it clearly happens in other countries as well; it is an international issue—I believe that science in this country is incredibly badly reported. I was thinking a lot about this last night but I think on reflection it is no worse reported than any of the other news! The whole premise on which we work today is—again to use a colloquial term—in terms of the "sound bite". If it is negative it is good because you can get a message over immediately and the whole way the public is fed information today is done in that way and so science is really no different. I think we have specific issues here that we should address and we can address and I think that industry should certainly play a part in this. I think government also has a role and that initially the targeting should be at the level of schools. The battleground is in the classroom. I do not think there is any doubt about that and the potential impact of biotechnology in terms of the health of the nation and the productivity of the nation needs to be got across to these people. We have less of a problem in terms of medicine than obviously they do in other areas but it is still trivialised. The whole reporting of it is trivialised. I think if only we could do something in terms of getting it across that scientists are serious about what we are doing and do think about the impact of our work; we would all benefit.

284. It costs a great deal of money to reach the general public in a general way the profits of

[Lord Perry of Walton *Cont*]
biotechnology are going to go to the industry rather than to the government.

(*Dr Ward*) With respect, I do not think it takes a great deal of money to get to the children in the classrooms. I think we could do a significant amount of work there for a relatively small amount of money.

Chairman

285. You mean the industry would do the work, do you?

(*Dr Ward*) I think industry is starting to do some work, yes. If we revert back to Lord Whaddon's comments in terms of animals, I think ABPI has done significant good work in terms of getting the risks of animal experimentation across to teachers and to children. They may not have been very effective yet but they are actually trying to do this. I think we need to so similar things in terms of biotechnology.

286. I think we have probably come to the end of our questions. Is there anything you would like to add at this point which we perhaps have not touched on which is of interest to you?

(*Dr Ward*) I think we have covered most of the things. I would make one final point, I think, that without doubt we, within Glaxo, see biotechnology as a vital sector as far as the United Kingdom is concerned. I think we must address the issues somehow, whether it is industry and government together, which I think is the way we should move forward; we must address the issues of being able to build on our traditional strengths of supporting the science base within the country in this particular area, and in improving the public perception, not only in biotechnology but of science as a whole.

(*Dr Weir*) I would echo that. I think the reason why we have a strong pharmaceutical and biotechnology sector here, relative to, say, other parts of Europe, is that we have a good traditional strength in molecular biology and structural biology. That is a critical strategic area in the country to maintain.

Lord Perry of Walton] That is the responsibility of government.

Chairman] I do not think we want to go into that at the moment, although we may later when we come to our report. Thank you very much for coming. If, when you receive a transcript of the evidence, you feel you want to amplify any points or add to it, we would be very pleased to hear from you. Thank you very much.

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